REMARKS

FORMAL MATTERS:

Claims 41-66 are pending after entry of the amendments set forth herein.

Claims 1-40 were canceled without prejudice.

Claim 66 is added.

Claims 41, 53, 54, 56-58 and 65 are amended.

Within the Advisory Action there was an objection with respect to support for the amendments offered to claim 41.

The amendments to claim 41 as well as new claim 66 are fully supported within Example 1 on pages 21 and 22 of the specification.

Example 1 describes a method in which cells are initially grown and then harvested. The harvest cells are dislodged from the flask or container collected in the centrifuge tube. The cells are then re-suspended in order to carry out a cell count which requires that the cells be individually separated. This is specifically disclosed at page 22, lines 3-6. The cells are then subjected to centrifugation, wherein the centrifugation causes aggregation of the cells as specifically described in Example 1. See Example 1 at page 21, lines 15-18 which reads as follows:

> Aggregation protocols for 2 hESC lines were established using two methods: aggregation by gravity and aggregation facilitated by centrifugation. Both protocols utilize serum-free media and low adhesion plates designed to facilitate formation of cellular aggregates.

Example 1 goes on to refer to further details of the process such as at page 21, lines 21-24 which read as follows:

> To ensure identification of the approximate number of cells that would be present in the created aggregated bodies, the starting hESC cells were harvested, suspended in serum-free media, and the concentration of the cells determined as described below.

On page 22, at lines 4-7 the Example goes on to describe the following:

> The cells were gently resuspended in 3-5 mls of the differentiation medium base (without growth factors), and a cell count performed. A sample of the resuspended hESCs was used to determine the approximate concentration of the hESC in the resuspension solution.

In order to perform the cell count the cells must be individually separate as claimed within amended claim 41.

Example 1 goes on to describe additional details as follows:

> Additional differentiation media with growth factors added (see Table 1) was added to the cells to bring the total volume to a level resulting in the desired cell concentration. (see page 22, lines 11-12)

Finally Example 1 at page 22, lines 14-18 reads as follows:

> The cells were then either returned to the incubator (37°C, 5% CO_2 in air) and allowed to aggregate by gravity (Aggregation Technique 1) or, more commonly, aggregated by spinning the plates at 1500 rpm for 4 minutes at 4°C (Aggregation Technique 2). Following centrifugation, the wells were examined microscopically to ensure that the cell were aggregated in the wells.

The above clearly shows that Example 1 provides a complete description and enablement of the invention as claimed and specifically shows that the hESC were first resuspended to allow for a cell count to be performed. The cell count can only be determined once the hESCs are suspended as individual cells and one skilled in the art would readily recognize such. Thus, the suspension of hESCs that are subsequently subjected to centrifugation must, by inference, be made up of individually separated hESCs consistent with amended claim 41.

The amendments to claim 41 are made in order to clarify language previously included in the claim and clearly indicate that the suspension of cells is a suspension of individual separate cells. This is shown in the Examples such as in Example 1 bridging pages 21 and 22 of the specification.

Claim 53 is amended so that a multiple dependent claim is not dependent on another multiple dependent claim.

The amendment to claim 54 is made in response to a specific objection raised by the Examiner. The claim indicates that the cells are cultured in the presence of a culture medium as supported by the Examples.

Claim 56 is also amended in response to a specific objection to indicate that the cells are growing in a culture medium as shown in the Examples.

Claim 57 is amended to refer to the RPMs as being 1500 as supported in the specification at page 22, line 4.

Claim 58 is amended to correct a formal error and provide a proper antecedent basis for the term "growth factor" and is supported in the specification in the Examples such as on page 21, in the second to final line.

Claim 65 is also amended in response to a specific objection. The cells are cultured in the culture medium as supported in the Examples and the amendment reflects such. The cells are grown to 60-80% confluency as supported in the specification at page 21, line 21.

No new matter is added.

REJECTIONS UNDER §112, ¶1

Claims 57 and 65 were objected under 35 U.S.C. §112, first paragraph. The objection was specifically made with respect to number amounts included within the claims which the Examiner did not find within the specification. Both claims have been amended to include specific number amounts found in the specification. The comments above point out within the specification support for those number amounts. Accordingly, the rejections are believed to have been overcome.

REJECTIONS UNDER §112, ¶2

Claims 54-65 were rejected under 35 U.S.C. §112, second paragraph as being indefinite. In response to the specific objections each of the claims have been amended. Support for the amendment

in the Examples has been pointed out. In view of such the rejections are believed to have been overcome.

REJECTIONS UNDER §102

Claims 41-50 were rejected under 35 U.S.C. §102 as anticipated by U.S. Patent 6,602,711 to Thomson. The rejection is traversed as applied and as it might be applied to the presently pending claims.

The Thomson patent discloses colonies of cells which form clumps. Specifically, reference is made to col. 3, lines 62-65 which read as follows:

> One allows colonies to form clumps over a period of hours. ES cell colonies can then be removed from the tissue culture plate using physical or chemical methods that keep the ES cells in clumps.

Within amended claim 41 applicants claim obtaining a suspension of "individual separate hESCs and subjecting the suspended individual cells to centrifugation." Thomson et al. teach towards trying to keep the cells together in clumps and as such do not anticipate the claimed invention within the meaning of 35 U.S.C. §102. In view of such reconsideration and withdrawal of the rejection is respectfully requested.

REJECTIONS UNDER §103(A)

Claims 41 and 50-53 were rejected under 35 U.S.C. §103 as unpatentable over Thomson et al. and Kaufman. The rejection is traversed as applied and as it might be applied to presently pending claims.

Neither Thomson et al. or Kaufman et al. teach the basic step of obtaining a suspension of individual separate hESCs and subjecting the suspended individual cells to centrifugation. Thus, even if the Thomson et al. reference is combined with Kaufman there is no teaching of this basic step.

The primary reference to Thomson et al. teaches a method of producing primate embryoid bodies from colonies of primate embryonic stem cells adhered to a substrate. The adhered colonies are removed in "clumps" via chemical or mechanical means. The clumps are then incubated under non-attachment conditions to facilitate the formation of embryoid bodies. This procedure is clearly different

conceptually from applicants' invention which requires obtaining a suspension of individual separate cells and then subjecting that suspension to centrifugation.

Thomson et al. make it clear that the adhered colonies are carefully removed from the substrate so as to retain embryoid bodies in clumps (see col. 3, lines 62-65). Further, Thomson et al. make it clear that they are trying to keep all of the cells together in clumps as taught within Thomson et al. at col. 4, lines 9-10. Thus, in order to carry out the teachings of Thomson et al. the aggregates of cells is essential to the method being taught. The rejection which is based on a deviation from this destroys the invention being taught by Thomson et al. and as such does not support a rejection of the claims under 35 U.S.C. §102 or §103.

Unlike Thomson et al. or Kaufman et al. the present invention is directed to a method whereby a suspension of individualized hESCs is subjected to centrifugation to form an aggregate of hESCs. This method is described within Example 1 on pages 21 and 22 of the specification as pointed out below:

> *"hESCs grown on mouse food cells were passaged the day before the procedure and were used in the experiments at approximately 60-80% confluency. To ensure identification of the approximate number of cells that would be present in the created aggregated bodies, the starting hESC cells were harvested, suspended in serum-free media, and the concentration of the cells determined as described below...differentiation medium base (without growth factors...was added to each flask, and the hESCs dislodged from the flask by physically shaking the flask. The cells were then collected into a centrifuge tube and the cells spun at 1500 rpm, for 2 minutes at 4°C. The cells were gently resuspended in 3-5 ml of the differentiation medium base (without growth factors), and a cell count performed."*
>
> *"A sample of the resuspended hESCs was used to determine the approximate concentration of the hESCs in the resuspension solution."*

In accordance with applicants' invention one skilled in the art will recognize that to allow a cell count to be performed hESCs must be resuspended as individualized cells in the differentiation medium base. This is because any aggregates will interfere with the cell count. This is completely different from what is being taught in the primary reference to Thomson et al. which requires the clumps of cells.

In the present application as page 22, lines 11-22 there is an indication that following the cell count, the total volume of hESC suspension is adjusted to a level so as to provide a desired hESC concentration. One skilled in the art would readily understand that a desired hESC concentration cannot be achieved if the hESCs are present in aggregates. In other words, obtaining a desired hESC

concentration of the population of the cells can only be obtained if the population of cells is prepared as a suspension of individualized cells. The limitation of the pending claims is not only not disclosed within the cited references but actually contrary to what is taught by Thomson et al. which requires only aggregates of ESCs (in the form of embryoid bodies) be subjected to centrifugation.

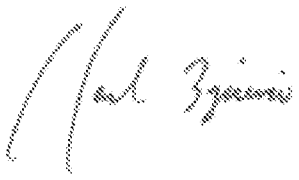
In view of the above and the claim amendments reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number DVCC-009.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP



Date: 7 June 2011 By: _____
Karl Bozicevic
Registration No. 28,807

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, California 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231